

WHAT IS CLAIMED IS:

1. A method for identifying an agent that reduces CMV dissemination in an animal, the assay comprising determining whether the agent inhibits the expression or activity of US28 or a US28 homolog, or a fragment or a variant of US28 or the US28 homolog.

2. The method of claim 1, wherein the US28 homolog is selected from the group consisting of human UL33, human UL33 spliced, human UL78, rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, rhUL33 spliced and rhUL78.

3. The method of claim 1, wherein the determining step comprises
(a) contacting a chemokine and US28, the US28 homolog, the fragment or the variant in the presence of the agent; and
(b) determining whether the agent inhibits binding between the chemokine and US28, the US28 homolog, the fragment or the variant.

4. The method of claim 3, wherein the chemokine is a CX3C chemokine.

5. The method of claim 4, wherein the chemokine is fractalkine.

6. The method of claim 3, wherein the chemokine is a CC chemokine.

7. The method of claim 6, wherein the chemokine is selected from the group consisting of MIP-1 α , MIP-1 β , MCP-1, eotaxin, vMIP-2 and RANTES.

8. The method of claim 3, wherein the agent is an antibody that specifically binds to US28, the US28 homolog, the fragment or the variant.

9. The method of claim 3, wherein the agent is a small molecule.

10. The method of claim 1, wherein the determining step comprises

(a) contacting a cell expressing US28, the US28 homolog, the fragment or the variant with a chemokine in the presence of the agent; and

(b) determining whether the agent inhibits binding between the chemokine and US28, the US28 homolog, the fragment or the variant.

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11. The method of claim 10, wherein the cell is infected with CMV.

12. The method of claim 10, wherein the cell is transfected with a heterologous nucleic acid encoding US28, the US28 homolog, the fragment or the variant.

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13. The method of claim 12, wherein US28, the US28 homolog, the fragment or the variant comprises at least 10 contiguous amino acids from the group of amino acid sequences as shown in SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24 or 26 and binds to the chemokine.

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14. The method of claim 10, wherein the chemokine is a CX3C chemokine.

15. The method of claim 14, wherein the chemokine is fractalkine.

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16. The method of claim 10, wherein the chemokine is a CC chemokine.

17. The method of claim 16, wherein the chemokine is selected from the group consisting of MIP-1 α , MIP-1 β , MCP-1, eotaxin, vMIP-2 and RANTES.

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18. The method of claim 10, wherein the agent is an antibody that specifically binds to US28, the US28 homolog, the fragment or the variant.

19. The method of claim 10, wherein the agent is a small molecule.

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20. The method of claim 1, wherein the determining step comprises

(a) administering the agent to a non-human animal infected with CMV;

and

(b) determining whether the agent inhibits the dissemination of CMV from a primary site of infection in the non-human animal.

21. The method of claim 20, wherein the animal is a non-human primate.

22. The method of claim 21, wherein the primate is a rhesus monkey, the CMV is rhCMV and the US28 homolog is selected from the group of rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, rhUL33 spliced and rhUL78.

23. The method of claim 20, wherein the agent is an antibody that specifically binds to the US28 homolog.

24. The method of claim 20, wherein the agent is an antisense nucleic acid that specifically hybridizes to a segment of a nucleic acid encoding the US28 homolog or a ribozyme that specifically recognizes a nucleic acid encoding the US28 homolog.

25. The method of claim 20, wherein the agent is a small molecule.

26. The method of claim 20, wherein the determining step (b) comprises determining whether viral titer in a saliva, urine or blood sample obtained from the non-human animal is detectably less than viral titer in a corresponding sample obtained from the saliva, urine or blood of a control animal.

27. The method of claim 20, wherein the determining step (b) comprises
(i) obtaining a peripheral blood sample from the non-human animal;
(ii) amplifying a region of CMV which is present in the sample with a set of primers that specifically hybridize to a segment of the CMV genome to form amplified product; and
(iii) detecting amplified product.

28. The method of claim 20, wherein the determining step (b) comprises obtaining a tissue sample from the non-human animal and staining the tissue with an antibody that specifically binds to CMV.

29. The method of claim 20, wherein the determining step (b) comprises detecting activated T cells and/or memory cells in a peripheral blood sample taken from the non-human animal.

5 30. A method for treating an animal infected with cytomegalovirus (CMV) or at risk for infection by cytomegalovirus (CMV), comprising administering to the animal an agent that interferes with the expression or activity of US 28 or a US28 homolog.

10 31. The method of claim 30, wherein the animal is a human and the US28 homolog is selected from the group consisting of human UL33, human UL33 spliced and human UL78.

32. The method of claim 31, wherein the US28 homolog is human UL33.

15 33. The method of claim 31, wherein the US28 homolog is human UL78.

34. The method of claim 30, wherein the animal is a rhesus monkey and the US28 homolog is selected from the group consisting of rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, rhUL33 spliced and rhUL78.

20 35. The method of claim 34, wherein the US28 homolog is rhUS28.1.

36. The method of claim 34, wherein the US28 homolog is rhUS28.2.

25 37. The method of claim 34, wherein the US28 homolog is rhUS28.3.

38. The method of claim 34, wherein the US28 homolog is rhUS28.4.

39. The method of claim 34, wherein the US28 homolog is rhUS28.5.

30 40. The method of claim 34, wherein the US28 homolog is rhUL33.

41. The method of claim 34, wherein the US28 homolog is rhUL78.

42. The method of claim 30, wherein the agent interferes with expression of a target nucleic acid encoding US28 or the US28 homolog in cells of the animal.

5 43. The method of claim 42, wherein interference is achieved by administering an antisense nucleic acid that specifically hybridizes to the target nucleic acid.

44. The method of claim 42, wherein interference is achieved by administering a ribozyme that specifically recognizes the target nucleic acid.

10 45. The method of claim 42, wherein the target nucleic acid encodes US28.

46. The method of claim 42, wherein the target nucleic acid encodes human UL33 or human UL78.

15 47. The method of claim 42, wherein the target nucleic acid encodes rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, rhUL33 spliced or rhUL78.

20 48. The method of claim 30, wherein the agent inhibits the binding of a chemokine to US28 or the US28 homolog.

25 49. The method of claim 48, wherein the agent is an antibody that specifically binds to US28 or the US28 homolog.

50. The method of claim 48, wherein the agent is a small molecule.

51. The method of claim 48, wherein the agent inhibits binding of the chemokine to US28.

30 52. The method of claim 48, wherein the US28 homolog is human UL33 or human UL78.

53. The method of claim 48, wherein the US28 homolog is rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, rhUL33 spliced or rhUL78.

54. The method of claim 48, wherein the chemokine is a CX3C chemokine.

55. The method of claim 54, wherein the chemokine is fractalkine.

5 56. The method of claim 48, wherein the chemokine is a CC chemokine.

57. The method of claim 56, wherein the chemokine is selected from the group consisting of MIP-1 α , MIP-1 β , MCP-1, eotaxin, vMIP-2 and RANTES.

10 58. The method of claim 30, wherein the agent is a vaccine which generates an immune response in the animal, and wherein the vaccine is attenuated through inhibition of expression or activity of US28 or US28 homolog.

15 59. The method of claim 58, wherein the vaccine comprises an immunogenic HCMV polypeptide encoded by at least a region of an HCMV genome in which the polynucleotide segment encoding US28 has been inactivated.

20 60. The method of claim 58, wherein the vaccine comprises an immunogenic HCMV polypeptide encoded by at least a region of an HCMV genome in which the polynucleotide segment encoding human UL33 or human UL78 has been inactivated.

25 61. The method of claim 58, wherein the vaccine comprises an immunogenic rhCMV polypeptide encoded by at least a region of a rhCMV genome in which the polynucleotide segment encoding rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, or rhUL78 has been inactivated.

62. The method of claim 30, wherein CMV titer is reduced by 5-fold or greater as measured in blood, saliva, or urine following administration of the agent.

30 63. The method of claim 30, wherein interference results in a delay in appearance or reduction of levels of reactive leukocytes in the peripheral blood of the animal.

64. An isolated, purified or recombinant nucleic acid that encodes a protein that is a US28 homolog, wherein said protein

- (a) has an amino acid sequence at least 75% identical to an amino acid sequence selected from the group consisting of SEQ ID NOS:6, 8, 10, 12, 14, 18, 24 and 26; and
- (b) binds a chemokine.

65. The nucleic acid of claim 64, wherein the protein has a sequence selected from the group consisting of SEQ ID NOS:6, 8, 10, 12, 14, 18, 24 and 26.

66. The nucleic acid of claim 64, wherein the nucleic acid has a sequence selected from the group consisting of SEQ ID NOS:5, 7, 9, 11, 13, 17, 23 and 25.

67. A vector comprising the nucleic acid of claim 64.

68. A cell comprising the nucleic acid of claim 64.

69. An isolated or recombinant protein comprising an amino acid sequence having at least 75% identical to an amino acid sequence as set forth in SEQ ID NOS:6, 8, 10, 12, 14, 18, 24 or 26 over a region at least 40 amino acids in length, and wherein the protein can bind a chemokine.

70. The protein of claim 69, that is encoded by a nucleic acid segment that hybridizes under stringent conditions to a nucleic acid having a sequence selected from the group consisting of SEQ ID NOS:5, 7, 9, 11, 13, 17, 23 and 25.

71. An isolated protein comprising at least 12 amino acids from one of the sequences set forth in SEQ ID NOS:6, 8, 10, 12, 14, 18, 24 or 26.

72. A vaccine, comprising

- (a) an immunogenic CMV polypeptide which is encoded by at least a region of a CMV genome in which the polynucleotide segment encoding US28 or a US28 homolog has been inactivated; and
- (b) a pharmaceutically acceptable carrier.

73. The vaccine of claim 72, wherein the immunogenic CMV polypeptide is an HCMV polypeptide encoded by at least a region of an HCMV genome in which the polynucleotide segment encoding US28 has been inactivated.

74. The vaccine of claim 72, wherein the immunogenic CMV polypeptide is an HCMV polypeptide encoded by at least a region of an HCMV genome in which the polynucleotide segment encoding human UL33 or human UL78 has been inactivated.

75. The vaccine of claim 72, wherein the immunogenic CMV polypeptide is a rhCMV polypeptide encoded by at least a region of a rhCMV genome in which the polynucleotide segment encoding rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4, rhUS28.5, rhUL33, or rhUL78 has been inactivated.

76. The vaccine of claim 75, wherein the immunogenic CMV polypeptide is a rhCMV polypeptide encoded by at least a region of a rhCMV genome in which the polynucleotide segment encoding rhUS28.1, rhUS28.2, rhUS28.3, rhUS28.4 or rhUS28.5 is inactivated.

add β3

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